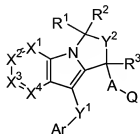


**Amendment to the Claims:**

Please amend Claims 1, 6, 15 and 20, and cancel Claims 3, 7 and 22-26 as follows.

**Listing of Claims:**

1. (Twice Amended) A compound having the formula I



I

and pharmaceutically acceptable salts and hydrates thereof, wherein:

A is selected from C<sub>1-3</sub>alkyl optionally substituted with one to four halogen atoms, O(CH<sub>2</sub>)<sub>1-2</sub>, and S(CH<sub>2</sub>)<sub>1-2</sub>;

Ar is ~~aryl or heteroaryl each optionally substituted with one to four groups independently selected from R<sup>6</sup>~~ selected from phenyl, 2-, 3-, 4-chlorophenyl, 2-, 3-, 4-bromophenyl, 2-, 3-, 4-fluorophenyl, 3,4-dichlorophenyl, 2,3-dichlorophenyl, 2,4-dichlorophenyl, 2,5-dichlorophenyl, 2,6-dichlorophenyl, 3,5-dichlorophenyl, 3-chloro-4-fluorophenyl, 2-chloro-4-fluorophenyl, 4-chloro-2-fluorophenyl, 2-cyanophenyl, 4-methylphenyl, 4-isopropylphenyl, 4-trifluoromethylphenyl, biphenyl, naphthyl, 3-methoxyphenyl, 3-carboxyphenyl, 2-carboxamidophenyl, 4-methoxyphenyl, 3-phenoxyphenyl, 4-(4-pyridyl)phenyl, 4-methylsulfonylphenyl, 3-dimethylaminophenyl, 5-tetrazolyl, 1-methyl-5-tetrazolyl, 2-methyl-5-tetrazolyl, 2-benzothienyl, 2-benzofuranyl, 2-indolyl, 2-quinoliny, 7-quinoliny, 2-benzothiazolyl, 2-benzimidazolyl, 1-benzotriazolyl, 2-furanyl, 3-furanyl, 2-imidazolyl, 5-imidazolyl, 5-isoxazolyl, 4-isoxazolyl, 4-isothiazolyl, 1,2,4-oxadiazol-5-yl, 2-oxazolyl, 4-oxazolyl, 4-pyrazolyl, 5-pyrazolyl, 2-pyridyl, 3-pyridyl, 2-pyrazinyl, 5-pyrimidinyl, 2-pyrrolyl, 4-thiazolyl, 1,2,4-thiadiazol-3-yl, 1,2,5-thiadiazol-4-yl, 1,2,3-thiadiazol-4-yl, 1,2,5-oxadiazol-4-yl, 1,2,3-oxadiazol-4-yl, 1,2,4-triazol-5-yl, 1,2,3-triazol-4-yl, 3-thienyl, 1,2,4-triazol-5-yl, pyrrolopyridine, furo[3,2-b]pyridin-2-yl, thieno[2,3-b]pyridin-2-yl, 5(H)-2-oxo-4-furanyl, 5(H)-2-oxo-5-furanyl, (1H,4H)-5-oxo-1,2,4-triazol-3-yl, 4-oxo-2-benzopyranyl;

Q is COOH,

one of  $X^1$ ,  $X^2$ , or  $X^3$  or  $X^4$  is nitrogen and the others are independently selected from CH and C-R<sub>g</sub> and R<sub>g</sub> is selected from 1) C<sub>1-6</sub>alkyl optionally substituted with one to eight groups independently selected from aryl, heteroaryl, halogen, NR<sup>a</sup>R<sup>b</sup>, C(O)R<sup>a</sup>, C(OR<sup>a</sup>)R<sup>a</sup>R<sup>b</sup>, SR<sup>a</sup> and OR<sup>a</sup>, wherein aryl, heteroaryl and alkyl are each optionally substituted with one to six groups independently selected from halogen, CF<sub>3</sub>, and COOH; or 2) S(O)<sub>n</sub>C<sub>1-6</sub>alkyl, wherein alkyl is optionally substituted with one to six substituents selected from halogen, aryl, heteroaryl, OH, and OC(O)R<sup>a</sup>;

X<sup>2</sup> is CH;

X<sup>4</sup> is CH or C-R<sub>g</sub>, where R<sub>g</sub> is selected from 1) C<sub>1-6</sub>alkyl optionally substituted with OR<sup>a</sup> or 2) S(O)<sub>n</sub>C<sub>1-6</sub>alkyl;

Y<sup>1</sup> is S;

Y<sup>2</sup> is selected from (CR<sup>d</sup>R<sup>c</sup>)<sub>m</sub> and CR<sup>d</sup>=CR<sup>c</sup>;

R<sup>1</sup> is selected from H, CN, OR<sup>a</sup>, S(O)<sub>n</sub>C<sub>1-6</sub>alkyl and C<sub>1-6</sub>alkyl optionally substituted with one to six groups independently selected from halogen, OR<sup>a</sup> and S(O)<sub>n</sub>C<sub>1-6</sub>alkyl;

R<sup>2</sup> is selected from H and C<sub>1-6</sub>alkyl optionally substituted with one to six halogen; or

R<sup>3</sup> is selected from H and C<sub>1-6</sub>alkyl optionally substituted with one to six groups independently selected from OR<sup>a</sup> and halogen;

R<sup>a</sup> and R<sup>b</sup> are independently selected from H; and C<sub>1-10</sub>alkyl, C<sub>2-10</sub>alkenyl, C<sub>2-10</sub>alkynyl, Cy and Cy-C<sub>1-10</sub>alkyl, wherein said alkyl, alkenyl, alkynyl and Cy are optionally substituted with one to six substituents independently selected from halogen, amino, carboxy, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkoxy, aryl, heteroaryl, aryl-C<sub>1-4</sub>alkyl, hydroxy, CF<sub>3</sub>, OC(O)C<sub>1-4</sub>alkyl, OC(O)NR<sup>i</sup>R<sup>j</sup>, and aryloxy; or

R<sup>e</sup> is selected from C<sub>1-6</sub>alkyl optionally substituted with one to six halogen, aryl and heteroaryl, wherein said aryl and heteroaryl are optionally substituted with one to three groups selected from halogen, OC<sub>1-6</sub>alkyl, O-haloC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkyl and haloC<sub>1-6</sub>alkyl;

R<sup>d</sup> and R<sup>c</sup> are independently H, halogen, aryl, heteroaryl, C<sub>1-6</sub>alkyl or haloC<sub>1-6</sub>alkyl;

R<sup>f</sup> is selected from H, C<sub>1-6</sub>alkyl, haloC<sub>1-6</sub>alkyl, Cy, C(O)C<sub>1-6</sub>alkyl, C(O)haloC<sub>1-6</sub>alkyl, and C(O)-Cy;

R<sub>g</sub> is selected from

(1) —halogen;

(2) —CN;

(3) —C<sub>1-6</sub>alkyl optionally substituted with one to eight groups

independently selected from aryl, heteroaryl, halogen, NR<sup>a</sup>R<sup>b</sup>,

C(O)R<sup>a</sup>, C(OR<sup>a</sup>)R<sup>a</sup>R<sup>b</sup>, SR<sup>a</sup> and OR<sup>a</sup>, wherein aryl, heteroaryl and

- alkyl are each optionally substituted with one to six groups independently selected from halogen,  $\text{CF}_3$ , and  $\text{COOH}$ ;
- (4)  $\text{C}_{2-6}$ alkenyl optionally substituted with one to six groups independently selected from halogen and  $\text{OR}^a$ ;
- (5)  $\text{Cy}$
- (6)  $\text{C}(\text{O})\text{R}^a$ ;
- (7)  $\text{C}(\text{O})\text{OR}^a$ ;
- (8)  $\text{CONR}^a\text{R}^b$ ;
- (9)  $\text{OCONR}^a\text{R}^b$ ;
- (10)  $\text{OC}_{1-6}$ alkyl, wherein alkyl is optionally substituted with one to six substituents selected from halogen, aryl, heteroaryl, OH, and  $\text{OC}(\text{O})\text{R}^a$ ;
- (11)  $\text{O-Cy}$ ;
- (12)  $\text{S}(\text{O})_m\text{C}_{1-6}$ alkyl, wherein alkyl is optionally substituted with one to six substituents selected from halogen, aryl, heteroaryl, OH, and  $\text{OC}(\text{O})\text{R}^a$ ;
- (13)  $\text{S}(\text{O})_m\text{Cy}$ ;
- (14)  $\text{NR}^a\text{S}(\text{O})_m\text{R}^b$ ;
- (15)  $\text{NR}^a\text{R}^b$ ;
- (16)  $\text{NR}^a\text{C}(\text{O})\text{R}^b$ ;
- (17)  $\text{NR}^a\text{C}(\text{O})\text{OR}^b$ ;
- (18)  $\text{NR}^a\text{C}(\text{O})\text{NR}^a\text{R}^b$ ;
- (19)  $\text{S}(\text{O})_m\text{NR}^a\text{R}^b$ ;
- (20)  $\text{NO}_2$ ;
- (21)  $\text{C}_{5-8}$ cycloalkenyl;

wherein Cy is optionally substituted with one to eight groups independently selected from halogen,  $\text{C}(\text{O})\text{R}^a$ ,  $\text{OR}^a$ ,  $\text{C}_{1-3}$ alkyl, aryl, heteroaryl and  $\text{CF}_3$ ;

$\text{R}^i$  and  $\text{R}^j$  are independently selected from hydrogen,  $\text{C}_{1-10}$ alkyl, Cy and  $\text{Cy-C}_{1-10}$ alkyl; or  $\text{R}^i$  and  $\text{R}^j$  together with the nitrogen atom to which they are attached form a ring of 5 to 7 members containing 0-2 additional heteroatoms independently selected from oxygen, sulfur and N- $\text{R}^k$ ;

Cy is selected from heterocyclyl, aryl, and heteroaryl;

m is 1 or 2; and

n is 0, 1 or 2.

2. (Original) A compound of Claim 1 wherein A-Q is  $\text{CH}_2\text{CO}_2\text{H}$ .
3. (Cancel)

4. (Previously Canceled)

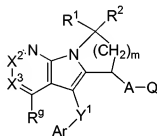
5. (Previously Canceled)

6. (Amended) A compound of Claim 1 wherein one of  $X^1$ ,  $X^2$  and  $X^3$  is nitrogen and the other is ~~others are~~ CH,  $X^2$  is CH, and  $X^4$  is C-S(O)<sub>n</sub>-C<sub>1-6</sub>alkyl or C-C<sub>1-6</sub>alkyl optionally substituted with OR<sup>a</sup>.

7. (Cancel)

8. (Original) A compound of Claim 1 wherein  $Y^2$  is selected from CH<sub>2</sub> and CH<sub>2</sub>CH<sub>2</sub>.

9. (Original) A compound of Claim 1 represented by the formula Ia:



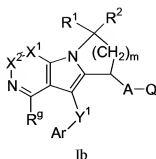
Ia

wherein  $X^2$  and  $X^3$  are independently CH or C-R<sub>g</sub>, A, Ar, Q,  $Y^1$ ,  $R^1$ ,  $R^2$ , m and R<sub>g</sub> are as defined in Claim 1.

10. (Original) A compound of Claim 9 wherein  $X^2$  and  $X^3$  are each CH,  $R^1$  and  $R^2$  are each H, and A-Q is CH<sub>2</sub>CO<sub>2</sub>H.

11. (Original) A compound of Claim 9 wherein  $Y^1$ -Ar is S-phenyl optionally substituted with 1 or 2 groups independently selected from halogen, C<sub>1-6</sub> alkyl and trifluoromethyl.

12. (Original) A compound of Claim 1 represented by the formula Ib:

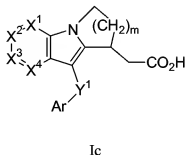


wherein X<sup>1</sup> and X<sup>2</sup> are independently CH or C-Rg, A, Ar, Q, Y<sup>1</sup>, R<sup>1</sup>, R<sup>2</sup>, m and Rg are as defined in Claim 1.

13. (Original) A compound of Claim 12 wherein X<sup>1</sup> and X<sup>2</sup> are each CH, R<sup>1</sup> and R<sup>2</sup> are each H, and A-Q is CH<sub>2</sub>CO<sub>2</sub>H.

14. (Original) A compound of Claim 13 wherein Y<sup>1</sup>-Ar is S-phenyl optionally substituted with 1 or 2 groups independently selected from halogen, C<sub>1</sub>-6 alkyl and trifluoromethyl.

15. (Amended) A compound of Claim 1 represented by the formula Ic:



wherein one of X<sup>1</sup>, ~~X<sup>2</sup>~~ and X<sup>3</sup> is N and the others ~~are each~~ is CH, ~~X<sup>4</sup> is CH~~, X<sup>4</sup> is CRg, m is 1 or 2, and Ar, Y<sup>1</sup> and m are as defined in Claim 1.

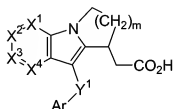
16. (Original) A compound of Claim 15 wherein Ar is phenyl optionally substituted with 1 or 2 groups independently selected from halogen, C<sub>1</sub>-3alkyl and trifluoromethyl.

17. (Previously Canceled)

18. (Original) A compound of Claim 15 wherein X<sup>4</sup> is selected from C-S(O)<sub>n</sub>-C<sub>1-6</sub>alkyl and C-C<sub>1-6</sub>alkyl optionally substituted with OR<sup>a</sup>.

19. (Previously Amended) A compound of Claim 15 wherein Y<sup>1</sup>-Ar is S-phenyl optionally substituted with 1 or 2 groups independently selected from halogen, C<sub>1-6</sub>alkyl and trifluoromethyl; X<sup>1</sup> and X<sup>2</sup> are each CH, X<sup>3</sup> is N, m is 1 or 2, and X<sup>4</sup> is C-SO<sub>2</sub>C<sub>1-6</sub>alkyl or C-C<sub>1-6</sub>alkyl.

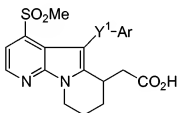
20. (Twice Amended) A compound of Claim 1 selected from:



X <sup>1</sup>	X <sup>2</sup>	X <sup>3</sup>	X <sup>4</sup>	Ar	Y <sup>1</sup>	m
N	CH	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	4-Cl-Ph	S	2
N	CH	CH	C(SCH <sub>3</sub> )	4-Cl-Ph	S	2
N	CH	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	3,4-diCl-Ph	S	2
N	CH	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	4-Br-Ph	S	2
CH	CH	N	C(SO <sub>2</sub> CH <sub>3</sub> )	3,4-diCl-Ph	S	1
CH	CH	N	C(SO <sub>2</sub> CH <sub>3</sub> )	3,4-diCl-Ph	S	2
N	CH	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	4-CF <sub>3</sub> -Ph	S	2
N	CH	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	2-Cl-4-F-Ph	S	2
N	CH	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	2-naphthyl	S	2
N	CH	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	2,3-diCl-Ph	S	2
N	CH	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	4-CH <sub>3</sub> -Ph	S	2
N	CH	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	Ph	S	2
N	CH	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	2,4-diCl-Ph	S	2
CH	N	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	4-Cl-Ph	S	2
CH	CH	N	C(SO <sub>2</sub> CH <sub>3</sub> )	4-Cl-Ph	S	2
N	C(CH <sub>3</sub> )	CH	C(SO <sub>2</sub> CH <sub>3</sub> )	4-Cl-Ph	S	2
N	CH	C(CH <sub>3</sub> )	C(SO <sub>2</sub> CH <sub>3</sub> )	4-Cl-Ph	S	2
CH	C(CH <sub>3</sub> )	N	C(SO <sub>2</sub> CH <sub>3</sub> )	4-Cl-Ph	S	2
C(CH <sub>3</sub> )	CH	N	C(SO <sub>2</sub> CH <sub>3</sub> )	4-Cl-Ph	S	2
N	CH	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-F-Ph	S	2

X <sup>1</sup>	X <sup>2</sup>	X <sup>3</sup>	X <sup>4</sup>	Ar	Y <sup>1</sup>	m
N	CH	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-Cl-Ph	S	2
N	CH	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	2,4-diCl-Ph	S	2
N	CH	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-Br-Ph	S	2
N	CH	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	2-Cl-4-F-Ph	S	2
N	CH	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	3,4-diCl-Ph	S	2
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-F-Ph	S	2
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-Cl-Ph	S	2
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	2,4-diCl-Ph	S	2
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-Br-Ph	S	2
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	2-Cl-4-F-Ph	S	2
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	3,4-diCl-Ph	S	2
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-F-Ph	S	1
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-Cl-Ph	S	1
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	2,4-diCl-Ph	S	1
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-Br-Ph	S	1
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	2-Cl-4-F-Ph	S	1
CH	CH	N	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	3,4-diCl-Ph	S	1
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-F-Ph	S	1
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-Cl-Ph	S	1
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	2,4-diCl-Ph	S	1
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-Br-Ph	S	1
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	2-Cl-4-F-Ph	S	1
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	3,4-diCl-Ph	S	1
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-F-Ph	S	2
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-Cl-Ph	S	2
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	2,4-diCl-Ph	S	2
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	4-Br-Ph	S	2
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	2-Cl-4-F-Ph	S	2
CH	N	CH	C(CH(CH <sub>3</sub> ) <sub>2</sub> )	3,4-diCl-Ph	S	2
N	CH	CH	C(CH(OCH <sub>3</sub> ) (CH <sub>2</sub> CH <sub>3</sub> ))	4-Cl-Ph	S	2
N	CH	CH	C(CH(OCH <sub>3</sub> ) (CH <sub>2</sub> CH <sub>3</sub> ))	4-Cl-Ph	S	1
CH	N	CH	C(CH(OCH <sub>3</sub> ) (CH <sub>2</sub> CH <sub>3</sub> ))	4-Cl-Ph	S	1

X <sup>1</sup>	X <sup>2</sup>	X <sup>3</sup>	X <sup>4</sup>	Ar	Y <sup>1</sup>	m
CH	N	CH	C(CH(OCH <sub>3</sub> ))(CH <sub>2</sub> CH <sub>3</sub> )	4-Cl-Ph	S	2
CH	CH	N	C(CH(OCH <sub>3</sub> ))(CH <sub>2</sub> CH <sub>3</sub> )	4-Cl-Ph	S	2
CH	CH	N	C(CH(OCH <sub>3</sub> ))(CH <sub>2</sub> CH <sub>3</sub> )	4-Cl-Ph	S	1
N	CH	CH	C(C(CH <sub>3</sub> ) <sub>3</sub> )	4-Cl-Ph	S	2
N	CH	CH	C(C(CH <sub>3</sub> ) <sub>3</sub> )	3,4-diCl-Ph	S	2
N	CH	CH	C(C(CH <sub>3</sub> ) <sub>3</sub> )	4-Br-Ph	S	2
N	CH	CH	C(C(CH <sub>3</sub> ) <sub>3</sub> )	4-CF <sub>3</sub> -Ph	S	2
N	CH	CH	C(C(CH <sub>3</sub> ) <sub>3</sub> )	2-Cl-4-F-Ph	S	2
N	CH	CH	C(C(CH <sub>3</sub> ) <sub>3</sub> )	2-naphthyl	S	2
N	CH	CH	C(C(CH <sub>3</sub> ) <sub>3</sub> )	2,3-diCl-Ph	S	2
N	CH	CH	C(C(CH <sub>3</sub> ) <sub>3</sub> )	4-CH <sub>3</sub> -Ph	S	2
N	CH	CH	C(C(CH <sub>3</sub> ) <sub>3</sub> )	Ph	S	2
N	CH	CH	C(C(CH <sub>3</sub> ) <sub>3</sub> )	2,4-diCl-Ph	S	2



Ar	Y <sup>1</sup>
5-tetrazolyl	S
2-pyrrolyl	S
1,2,4-triazol-3-yl	S
1,2,3-triazol-4-yl	S
5-imidazolyl	S
4-pyrazolyl	S
5-pyrazolyl	S
(1H,4H)-5-oxo-1,2,4-triazol-3-yl	S
4-isothiazolyl	S
1,2,5-thiadiazol-5-yl	S
1,2,5-oxadiazol-5-yl	S



Ar	Y <sup>1</sup>
3-furanyl	S
1,2,3-thiadiazol-4-yl	S
1,2,3-oxadiazol-4-yl	S
4-isoxazolyl	S
3-thienyl	S
4-oxazolyl	S
4-thiazolyl	S
(5H)-2-oxo-5-furanyl	S
(5H)-2-oxo-4-furanyl	S
1,2,4-oxadiazol-5-yl	S
3-pyridyl	S
2-pyrazinyl	S
5-pyrimidinyl	S
2-indolyl	S
2-benzothieryl	S
2-benzofuranyl	S
4-oxo-benzopyran-2-yl	S
2-quinolinyl	S
2-benzimidazolyl	S
2-benzoxazolyl	S
2-benzothiazolyl	S
1-benzotriazolyl	CH <sub>2</sub> S
thieno[2,3-b]pyridin-2-yl	S

21. (Original) A pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier.

22. (Cancel)

23. (Cancel)

24. (Cancel)

25. (Cancel)

26. (Cancel)

27. (Previously Canceled)

28. (Previously Canceled)

29. (Previously Canceled)

30. (Previously Canceled)